1. A method of assessing the efficacy of a compound of formula I in treating a treating a disease in a mammalian subject, or a cell derived therefrom, comprising:

measuring the expression or activity of Raf, VEGFR-2, VEGFR-3, p38, PDGFR-beta, and/or Flt-3 in a sample obtained from said subject who has been treated with a compound of formula I, and

determining the effects of said compound on said expression or activity,

wherein said compound of formula I is:

$$B\text{-}NH\text{-}C(O)\text{-}NH\text{-}L\text{-}M\text{-}L^1\text{-}(Q)_{1\text{-}3} \qquad (I)$$

wherein B is

(i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano, and nitro;

(ii) naphthyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano, and nitro;

(iii) a 5 or 6 membered monocyclic heteroaryl group, having 1-3 heteroatoms independently selected from the group consisting of O, N and S, optionally substituted with 1-3 substituents independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano, oxo, and nitro; or

(iv) an 8 to 10 membered bicyclic heteroaryl group in which the first ring is bonded to the NH of Figure I and contains 1-3 heteroatoms independently selected from the group consisting of O, N, and S, and the second ring is fused to the first ring using 3 to 4 carbon atoms. The bicyclic heteroaryl group is optionally substituted with 1-3 substituents independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano, oxo, and nitro.

L is

(i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, and nitro;

(ii) naphthyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, and nitro;

(iii) a 5 or 6 membered monocyclic heteroaryl group, having 1-3 heteroatoms independently selected from the group consisting of O, N and S, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, and nitro; or

(iv) an 8 to 10 membered bicyclic heteroaryl group having 1-6 heteroatoms independently selected from the group consisting of O, N and S, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, and nitro.

M is

(a) $-(CH_2)_m-O-(CH_2)_l-$,

(b) $-(CH_2)_m-(CH_2)_l-$,

(c) $-(CH_2)_m-C(O)-(CH_2)_l-$,

(d) $-(CH_2)_m-NR^3-(CH_2)_l-$,

(e) $-(CH_2)_m- NR^3C(O)-(CH_2)_l-$,

(f) $-(CH_2)_m-S-(CH_2)_l-$,

(g) $-(CH_2)_m-C(O)NR^3-(CH_2)_l-$,

(h) $-(CH_2)_m-CF_2-(CH_2)_l-$,

(i) $-(CH_2)_m-CCl_2-(CH_2)_l-$,

(j) $-(CH_2)_m-CHF-(CH_2)_l-$,

(k) $-(CH_2)_m-CH(OH)-(CH_2)_l-$;

(l) $-(CH_2)_m-C\equiv C-(CH_2)_l-$;

(m) $-(CH_2)_m-C=C-(CH_2)_l-$;

(n) $-(CH_2)_m-CR^4R^5-(CH_2)_l-$;

or

(o) a single bond, where m and l are 0;

wherein the variables m and l are integers independently selected from 0-4,

L' is

(i) phenyl, optionally substituted with 1-2 additional substituents other than Q, independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and nitro;

(ii) naphthyl, optionally substituted with 1-2 additional substituents other than Q, independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and nitro;

(iii) a 5 and 6 membered monocyclic heteroaryl group, having 1-3 heteroatoms independently selected from the group consisting of O, N and S, optionally substituted with 1-2 additional substituents other than Q, independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and nitro and also oxides (e.g. =O, $-O^-$ or –OH);

(iv) an 8 to 10 membered bicyclic heteroaryl group, having 1-6 heteroatoms independently selected from the group consisting of O, N and S, optionally substituted with 1-2 additional substituents other than Q, independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and nitro and also oxides (e.g. =O, $-O^-$ or –OH).

(v) a saturated and partially saturated C_3-C_6 monocyclic carbocyclic moiety optionally substituted with 1-2 additional substituents other than Q, independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and, nitro;

(vi) a saturated and partially saturated C_8-C_{10} bicyclic carbocyclic moiety, optionally substituted with 1-2 additional substituents other than Q, independently selected from the group

consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and nitro;

(vii) a saturated and partially saturated 5 and 6 membered monocyclic heterocyclic moiety, having 1-3 heteroatoms independently selected from the group consisting of O, N and S, optionally substituted with 1-2 additional substituents other than Q, independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2N$,$R^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and nitro, and also oxides (e.g. =O, $-O^-$ or –OH); or

(viii) a saturated and partially saturated 8 to 10 membered bicyclic heterocyclic moiety, having 1-6 heteroatoms independently selected from the group consisting of O, N and S, optionally substituted with 1-2 additional substituents other than Q, independently selected from the group consisting of R^1, OR^1, NR^1R^2, $S(O)_qR^1$, $SO_2NR^1R^2$, $NR^1SO_2R^2$, $NR^1C(O)R^2$, $NR^1C(O)OR^2$, halogen, cyano and nitro, and also oxides (e.g. =O, $-O^-$ or –OH); and

each Q is independently $C(O)R^4$, $C(O)OR^4$ and $C(O)NR^4R^5$;

wherein each R^1 - R^5 is independently selected from:

(a) hydrogen,

(b) C_1-C_5 linear, branched, or cyclic alkyl,

(c) phenyl,

(d) C_1-C_3 alkyl-phenyl, wherein the alkyl moiety is optionally substituted with halogen up to per-halo;

(e) up to per–halo substituted C_1-C_5 linear or branched alkyl. Or

(f) $-(CH_2)_q$-X, where X is a 5 or 6 membered monocyclic heterocyclic ring, containing 1-4 atoms selected from oxygen, nitrogen and sulfur, which is saturated, partially saturated, or aromatic, or a 8-10 membered bicyclic heteroaryl having 1-4 heteroatoms selected from the group consisting of O, N and S; and wherein said alkyl moiety is optionally substituted with halogen up to per-halo,

wherein each R^1 - R^5, other than per–halo substituted C_1-C_5 linear or branched alkyl, is optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3

alkoxy, hydroxy, carboxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, and nitro;

wherein the variable p is an integer selected from 0, 1, or 2 and the variable q is an integer selected from 0, 1, 2, 3, or 4.

2. A method of claim 1, wherein said measuring the expression is determining the amounts of mRNA corresponding to Raf, VEGFR-2, VEGFR-3, p38, PDGFR-beta, and/or Flt-3.

3. A method of claim 1, wherein said measuring the expression is determining the amounts of polypeptide corresponding to Raf, VEGFR-2, VEGFR-3, p38, PDGFR-beta, and/or Flt-3.

4. A method of claim 3, wherein said measuring the activity is determining the amounts of phospho-ERK.

5. A method of claim 4, wherein said subject has cancer, and measuring the activity is determining the amounts of phospho-ERK in peripheral blood lymphocytes or a tissue biopsy of a cancer.

6. A method of any of claims 1-5, further comprising comparing the expression or activity in said sample to a normal control.

7. A method of any of claims 1-6, further comprising comparing the expression or activity in at least one sample before treating with said compound and in at least one sample after treating with said compound.

8. A method of any of claims 1-7, further comprising measuring expression in at least two different samples collected at different timepoints in the treatment regimen with said compound.

9. A method of any of claims 1-8, wherein a reduction in expression or activity indicates that

said compound is effective in treating said disease.

10. A method of any of claims 1-9, wherein said disease is renal cell carcinoma or melanoma.

11. A method of any of claims 1-10, wherein said sample comprises tumor cells.

12. A method of any of claims 1-11, wherein said sample comprises peripheral blood cells.

13. A method of any of claims 1-11, further comprising administering a compound of formula I at a plurality of timepoints.

14. A method of selecting subjects having a disease for treatment with a compound of formula I, comprising:

measuring the expression or activity of Raf, VEGFR-2, VEGFR-3, p38, PDGFR-beta, and/or Flt-3, in a sample obtained from a subject having a disease, and administering said compound of formula I to subjects who are identified as having high levels of expression or activity, where said compound is a compound of formula I of claim 1.

15. A method of selecting subjects having a disease for treatment with a compound of formula I, comprising:

determining the the presence of a Raf, VEGFR-2, VEGFR-3, p38, PDGFR-beta, and/or Flt-3 gene mutation in a sample obtaiuned from a subject, wherein said mutation is associated with a disease, and

administering said compound of formula I of claim 1 to subjects who are identified as having said mutation.

16. A method of claim 15, wherein said mutation is in the BRAF gene.

17. A method of claim 16, wherein said BRAF mutation is at amino acid position 599 of the coding sequence of said gene.

18. A method of claim 17, wherein said BRAF mutation is V599E.

19. A method of any of claims 15-18, wherein said disease is melanoma.

20. A method for treating or preventing a disease or condition in mammal or a mammalian cell, comprising:

administering to a subject in need thereof, an effective amount of an aryl urea compound of formula I, a salt form of a compound of Formula I, an isolated or mixed stereoisomer of a compound of Formula I, an ester of a compound of formula I, a metabolite of a compound of formula I, or a prodrug of a compound of Formula I of claim 1.

21. A method of claim 20, wherein said method is for inhibiting tumor cell proliferation.

22. A method of claim 21, wherein said effective amount results in tumor regression.

23. A method of any of claims 20-22, wherein said method is causing tumor regression in a subject, or cells therefrom, having cancer.

24. A method of claim 20, wherein said method comprises inhibiting lymphangiogenesis.

25. A method of claim 20, wherein said method comprises inhibiting angiogenesis.

26. A method of claim 20, wherein said method comprises treating a disorder in a mammalian subject mediated by Raf, VEGFR-2, VEGFR-3, PDGFR-beta, and/or Flt-3.

27. A method of claim 20, wherein said method comprises treating a tumor in a subject in need thereof, comprising:

administering an effective amount of said compound wherein said amount is effective to inhibit tumor cell proliferation and neovascularization.

28. A method as in claim 1 wherein for the compounds of formula (I):

L is phenyl, optionally substituted with 1-4 halogen,

M is –O-,

B is phenyl or pyridyl, optionally substituted with 1-6 substituents independently selected from the group consisting of R^1 and halogen, and

L^1 is optionally substituted phenyl or pyridinyl.

29. A method as in claim 28 wherein the substituents on the groups for B and L' are selected from the group consisting of: methyl, ethyl, propyl, butyl, pentyl, isopropyl, isobutyl, *sec*-butyl, and *tert*-butyl, methoxy,ethoxy, F, Cl, Br, and I.

30. A method as in claim 1 wherein the pharmaceutically acceptable salt of a compound of formula I is selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

31. A method of assessing the efficacy of a compound in treating a disease in a mammalian subject, or a cell derived therefrom, comprising:

measuring the expression or activity of Raf, VEGFR-2, VEGFR-3, p38, PDGFR-beta, and/or Flt-3 in a sample obtained from said subject who has been treated with said compound, and

determining the effects of said compound on said expression or activity,

wherein said compound is:

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)-2-chlorophenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(1-hydroxy-2-carbamoyl-4-pyridyloxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(1-hydroxy-2-(N-methylcarbamoyl)-4-pyridyl oxy)phenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyl oxy)-2-fluorophenyl) urea,

N-(4-bromo-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyl oxy)-2-fluorophenyl) urea,

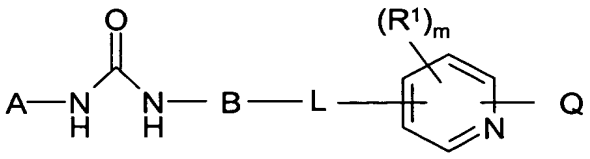
N-(4-fluoro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyl oxy)-2-fluorophenyl) urea,

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyl oxy)-2-chlorophenyl) urea,

N-(6-(2,2,4,4-tetrafluoro-4H-benzo[1,3]dioxinyl))-N'-(4-(2-cyano-4-pyridyloxy) phenyl) urea, or

N-(6-(2,2,4,4-tetrafluoro-4H-benzo[1,3]dioxinyl))-N'-(4-(2-cyano-4-pyridyloxy)-2-fluorophenyl) urea.

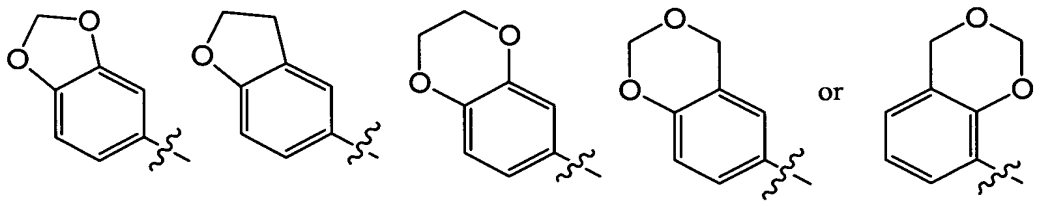
32. A method of claim 1 wherein the compound of formula I is of the formula X below,



(X)

wherein:

A is phenyl, optionally substituted 1, 2 or 3 times by R^3 , wherein each R^3 is independently C_1-C_5 alkyl, C_1-C_5 haloalkyl, up to per-haloalkyl, C_1-C_5 alkoxy, C_1-C_5 haloalkoxy, up to per-haloalkoxy, halogen, cyano, or nitro; or A is a group of the formula:



optionally substituted 1, 2, 3, 4, 5 or 6 times with R^4 wherein each R^4 is independently C_1-C_5 alkyl or halogen;

B is phenylene, optionally substituted 1, 2 or 3 times by R^2, or naphthylene, optionally substituted optionally substituted 1, 2 or 3 times by R^2, wherein each R^2 is independently C_1-C_5 alkyl, C_1-C_5 haloalkyl, up to per-haloalkyl, C_1-C_5 alkoxy, C_1-C_5 haloalkoxy up to per-haloalkoxyl, halogen, cyano or nitro;

Q is cyano, -C(O)-R^a, or -C(O)-NR^bR^c, where each R^a, R^b and R^c is independently H or C_1-C_5 alkyl,

L is -O- or -S-,

m is an integer 0,1,2 or 3, and

each R^1 is independently halogen, C_{1-5} alkyl, C_{1-5} haloalkyl, up to per-haloalkyl, C_{1-5} alkoxy, C_{1-5} haloalkoxy, up to per-haloalkoxy, N-oxo or N-hydroxy.

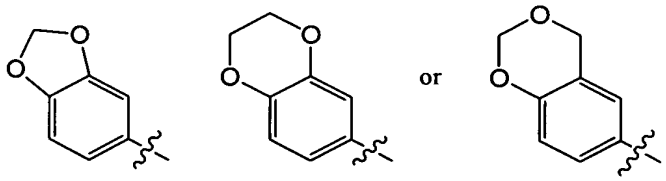
33. A method of claim 32 wherein for the compound of formula (X), each R^2 is independently fluorine, chorine, bromine, methyl, ethyl, propyl, butyl, isopropyl, tert-butyl, trifluoromethyl, methoxy, CN or NO_2.

34. A method of claims 32 or 33 wherein for the compound of formula (X), each R^3 is independently fluorine, chorine, bromine, methyl, ethyl, propyl, butyl, pentyl, isopropyl, iso-butyl, sec-butyl, tert-butyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, CN or NO_2 and each R^4 is independently fluorine, chorine, bromine or methyl.

35. A method of any of claims 32-34 wherein for the compound of formula (X), each R^1 is independently methyl, ethyl, propyl, oxygen, cyano, n-oxo or n-hydroxy and each R^a, R^b and R^c is independently H or methyl.

36. A method of claims 32-35 wherein for the compound of formula (X), A is substituted phenyl.

37. A method of any of claims 32-35 wherein for the compound of formula (X), A is a group of the formula:



optionally substituted 1, 2, 3 or 4 times with R^4, wherein each R^4 is independently chlorine or fluorine.

38. A method of any of claims 32-37 wherein for the compound of formula (X), B is phenylene.

39. A method of anyof claims 32-37 wherein for the compound of formula (X), B is naphthylene.

40. A method of any of claims 32-37 wherein for the compound of formula (X), B is phenylene substituted by at least one fluorine atom.

41. A method of any of claims 32-40 wherein for the compound of formula (X), L is oxygen.

42. A method of any of claims 32-41 wherein for the compound of formula (X), each R^3 is chlorine, bromine, tert-butyl, trifluoromethyl or methoxy.

43. A method of claim 32 wherein for the compound of formula (X),
A is 4-chloro-3-trifluoromethylphenyl, 4-fluoro-3-trifluoromethylphenyl, 4-bromo-3-trifluoromethylphenyl, or 2,2,4,4-tetrafluoro-4H-benzo[1,3]dioxin-6-yl;
B is phenylene, chlorophenylene or fluorophenylene;
L is -O-;
and
Q is cyano, C(O)-NH_2, or C(O)-NHMe.

44. A method of any of claims 32-43 wherein a pharmaceutically acceptable basic salt of an organic acid of a compound of formula (X) is used.

45. A method of claims 32-43 wherein a pharmaceutically acceptable basic salt of an organic acid of formula (X) is administered, selected from hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid.

46. The method of claim 32 wherein the compound of formula X is a pharmaceutically acceptable hydrochloride, benzenesulfonate, or methanesulfonate salt of

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-2-fluoro-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea or

N-(4-chloro-3-(trifluoromethyl)phenyl)-N'-(4-(2-(N-methylcarbamoyl)-4-pyridyloxy)phenyl) urea.

47. A method of assessing the efficacy of a compound in treating a treating a disease in a

mammalian subject, or a cell derived therefrom, comprising:

measuring the expression or activity of Raf, VEGFR-2, VEGFR-3, p38, PDGFR-beta, and/or Flt-3 in a sample obtained from said subject who has been treated with said compound , and

determining the effects of said compound on said expression or activity,

wherein said compound is

an aryl urea compound of formulae X, Y, ZA, ZB, ZC or ZD,

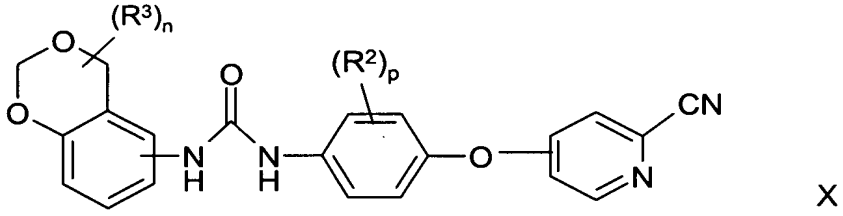
a salt form of a compound of formulae X, Y, ZA, ZB, ZC or ZD,

an isolated or mixed stereoisomer of a compound of formulae X, Y, ZA, ZB, ZC or ZD ,

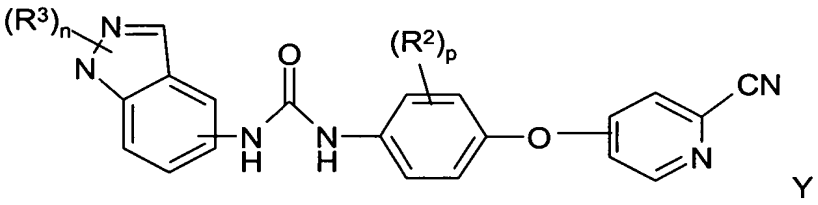
an ester of a compound of formulae X, Y, ZA, ZB, ZC or ZD,

a metabolite of a compound of formulae X, Y, ZA, ZB, ZC or ZD, or

a prodrug of a compound of formulae X, Y, ZA, ZB, ZC or ZD,

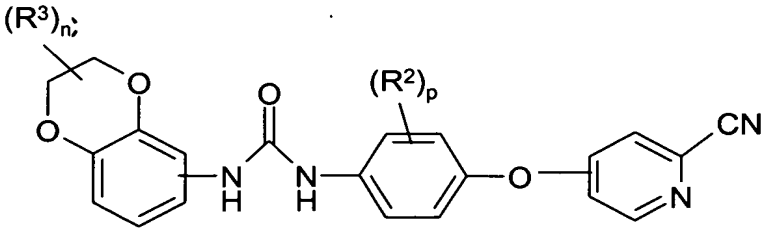


X

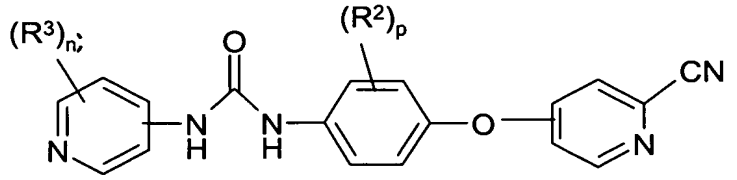


Y

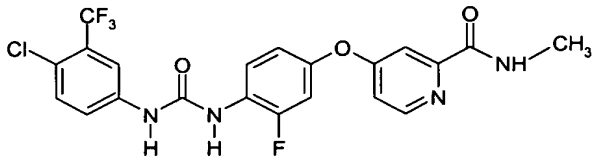
,



ZA

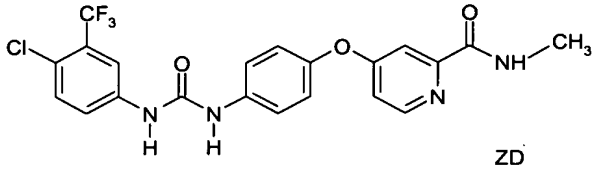


ZB



ZC

and



ZD

wherein

each R^3 is independently halogen or trifluoromethyl and

each R^2 is independently fluorine, chorine, bromine,

methyl, trifluoromethyl, methoxy, CN or NO_2.

the variable n is 0, 1, 2, 3 or 4 and

the variable p is 0 , 1 or 2.